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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COOLEY, CHARLES E	

ART UNIT	PAPER NUMBER
1723	

DATE MAILED: 10/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,855	SKINKLE ET AL.	
	Examiner	Art Unit	
	Charles E. Cooley	1723	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *37-39 and 42* is/are withdrawn from consideration.

5)☒ Claim(s) *40 and 41* is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☒ Claim(s) *36* is/are objected to.

8)☒ Claim(s) *1-42* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

NON-FINAL OFFICE ACTION

1. This application has been assigned to Technology Center 1700, Art Unit 1723 and the following will apply for this application:

Please direct all written correspondence with the correct application serial number for this application to Art Unit 1723.

Telephone inquiries regarding this application should be directed to the Electronic Business Center (EBC) at http://www.uspto.gov/ebc/index.html or 1-866-217-9197 or to the Examiner at (571) 272-1139. All official facsimiles should be transmitted to the centralized fax receiving number 571-273-8300.

Election/Restriction Requirement

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-36 and 40-41, drawn to a centrifuge apparatus comprising a mechanically actuated or spring-loaded bottom support plate, a fixed top support plate, an axial inlet/outlet attached to the top support plate by a rotating seal, a variable volume separation chamber, a pump and a rotary drive unit, as well as a method of processing blood in such a centrifuge.

Group II, claim(s) 37, drawn to a disposable cartridge comprising a plurality of ports and a fluid sensor pathway and being adapted to be mounted on a multi-position valve and adapted to be mounted adjacent to one or more sensors.

Group III, claim(s) 38-39, drawn to a disposable set comprising containers. a disk-shaped bag, a support plate with a seal assembly to attach an inlet/outlet thereto and tubing.

Group IV, claim(s) 42, drawn to a disposable bag comprising three compartments separated by perforated portions.

3. The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

There are no technical features in common between these groups of inventions. The features of the four different subject matters address different technical problems by means of different technical features.

The special technical feature of group I is the mechanically actuated or spring-loaded bottom support plate in order to maintain pressure on the variable volume separation chamber and to allow the bottom support plate to move vertically.

The special technical feature of group II is the assembly of the different parts into one cartridge in order to provide a compact device to be used with a centrifuge.

The special technical feature of group III is the set of the different parts which form together a single disposable set which allows easier handling.

The special technical feature of group IV is that the blood bag comprises three compartments separated by perforated portions in order to allow each compartment to be separated from the others.

4. During a telephone conversation with Patrick O'Connell on 23 SEP 2005 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-36 and 40-41. Affirmation of this election must be made by applicant in replying to this Office action. Claims 37-39 and 42 are thereby withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

6. Note the attached PTO-1449 forms submitted with the Information Disclosure Statements.

Specification

7. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

8. The abstract is acceptable.

9. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed (MPEP 606.01).

Claim Objections

10. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 28-41 have been renumbered as claims 29-42, respectively.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-14, 16-32, 34, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 2658926 A1 in view of Brown (US 4,530,691) and Cullis (US 4,734,089).

In accordance with the opinions in the ISA documents of 14 DEC 2004 and 31 MAR 2005, DE 2658926 A1 discloses a centrifuge apparatus and method as depicted below including a bottom support plate (2), a fixed top support plate (1), an axial inlet/outlet (see figures 1, 1a and 2) attached to the top support plate (1) by a rotating seal (6), a variable volume separation chamber (12) mounted between the support plates and fluidly connected to the axial inlet/outlet, a rotary drive unit (7) attached to the bottom support plate, as well as a method of processing blood in such a centrifuge.

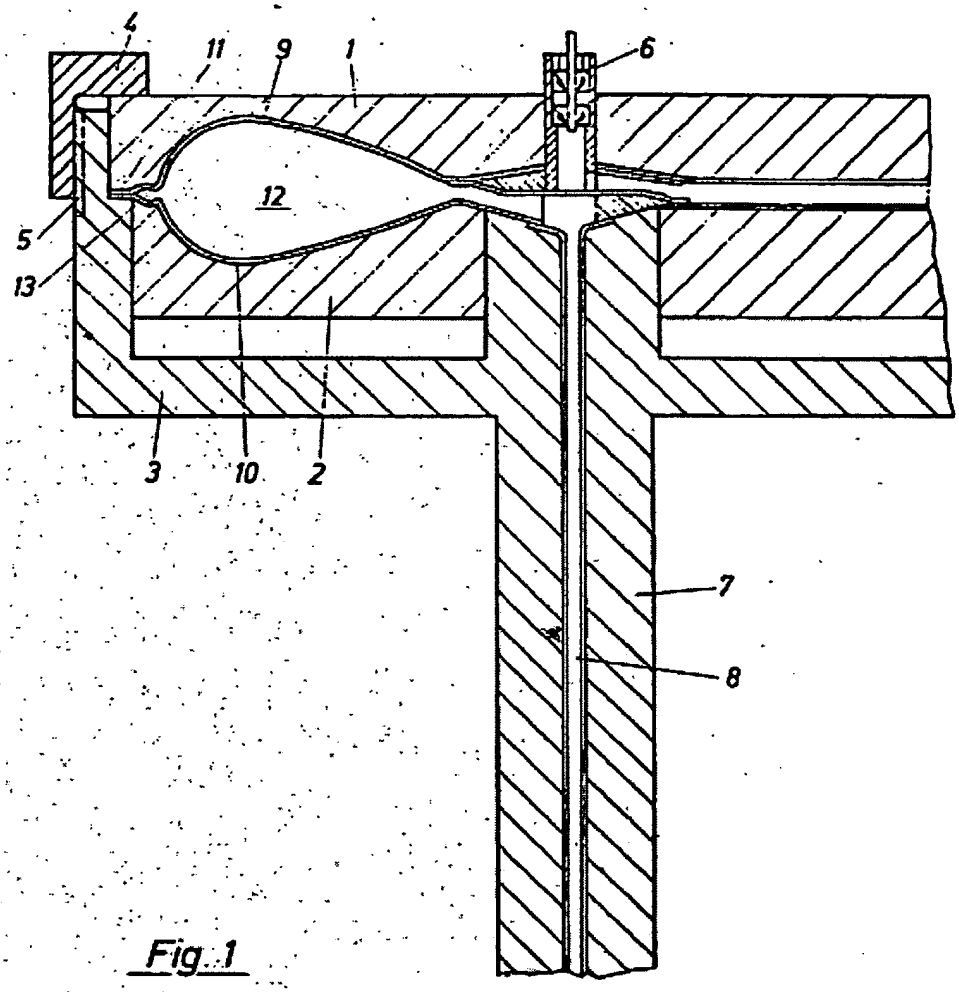


Fig. 1

Fig. 1a

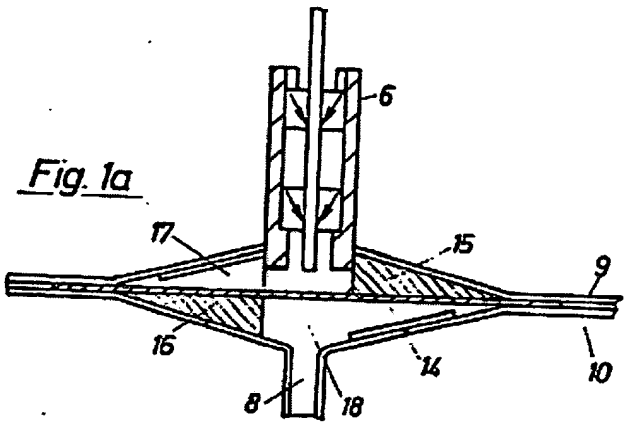
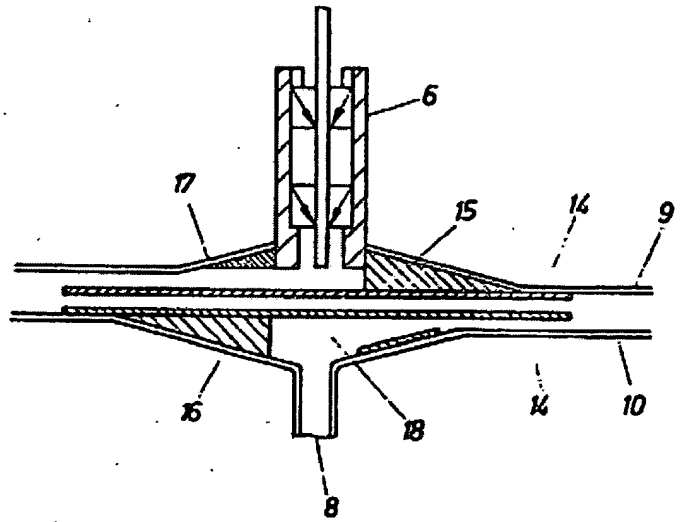


Fig. 2



DE 2658926 A1 seen above does not disclose the spring-loaded plate or the pump. With respect to the spring-loaded plate, the patent to Brown (US 4,530,691) discloses a centrifugal liquid processing apparatus for use in the onsite processing of whole blood into therapeutic constituents by centrifugal apheresis (e.g., plasmapheresis or plateletpheresis). The apparatus is particularly useful with a flexible, variable-volume, processing chamber and includes a chamber bowl or cover for receiving the processing chamber. A chamber-engaging mandrel is provided for engaging said chamber and causing the chamber to conform to the cover and for cooperation in controlling the volume of said chamber. The cover and mandrel are spun about a spin axis and the processing chamber spins therewith for separating the components. Fluid conduits are provided for connecting the chamber to the donor and to external sites for the collection of the therapeutic components.

The mandrel, cover and chamber cooperate to define a blood-collecting volume generally along the side walls of the chamber and a central plasma collecting volume at the base of the chamber. These volumes are substantially equal and remain equal as the total chamber volume changes.

Furthermore, the chamber is configured so that the surface area at which red blood cells will separate is greater than the surface area of the red blood cell/plasma interface. The result of the volume and surface area relationships is to maximize red blood cell (RBC) separation while minimizing platelet sedimentation back into the red blood cell bed or packed cell bed during RBC separation and collection.

Referring now to FIG. 1, an apparatus for centrifugal apheresis 10 generally is shown and includes a rotatable external assembly or housing 12 and a rotatable inner chamber support assembly 14 which carries the variable-volume chamber and movable mandrel. The housing 12 is generally cylindrical in shape and includes top and bottom half sections 16 and 18 which are connected by hinge 20. The bottom section 18 is connected to a drive system 22, which spins the outer housing at a first predetermined speed about a spin axis A--A. The top section 16 carries the inner chamber support assembly 14, which is positioned within the outer housing 12 and aligned with the spin axis A--A for rotation with the outer housing 12. An inner assembly drive 23 is mounted to the top section 16 and supports the chamber and cooperating members via drive shaft 24. The inner assembly drive spins the inner assembly 14 in the same direction as the outer assembly 12, but at twice the rate.

The inner assembly includes an inverted cup-shaped chamber support plate 28, which carries the chamber bowl or cover 30 and spring-biased chamber mandrel 32. A flexible, variable-volume, bowl-shaped chamber is positioned in the cover between the cover and mandrel, as best seen in FIGS. 2-4. A fluid conduit, which is sometimes referred to as an umbilicus 34, extends from the cover through the outer housing to a stationary external connection 36. The umbilicus can be either a single or multi-lumen tube.

The cover 30 is fixed to the chamber support plate 28 by a removable band 38 which releasably secures the cover to the support plate. Both the outer and inner housings are substantially symmetric about the central spin axis A--A, and during

operation, the chamber conforms to the shape of the mandrel and cover and assumes a generally axially symmetric shape.

Referring to FIG. 2, the processing chamber, which is a flexible, variable-volume, bowl-shaped member 40, is shown with a fluid communication port 42. This port is to be located on the spin axis A--A and is referred to as the low-gravity (low-G) port. In some systems a port is also located at the radially outermost point and is referred to as the high-G port. In a distended shape the chamber has a bladder-like shape that can be formed to the bowl-like shape.

In order to mount the chamber to the support assembly, the top section 16 of the outer housing is swung open about hinge 20 to an inverted horizontal position, the retainer band 38 is removed, and the chamber bowl cover is removed as shown in FIG. 2. Thereafter, a flexible, variable-volume chamber 40 is fitted to the mandrel 32 by rolling the chamber thereon. This chamber 40 has been fabricated from two heat-sealed and vacuum-formed polyvinylchloride sheets. The sealing flange 44 is shown engaging the support plate 28.

In a sense, the chamber is fitted to the mandrel as a glove is fitted to a hand. In this inverted position the mandrel is extended under a biasing action, but its movement is limited by the drive shaft. After the chamber is fitted to the mandrel, the bowl cover 30 is refitted and secured with the retainer band and the top section is returned to its closed position.

FIG. 3 shows the fully assembled inner assembly with the variable-volume chamber in place. More specifically, the internal drive 23 is supported by the outer

housing top section 16. The drive shaft 24 is aligned with the spin axis A--A and extends downwardly from the drive 23 through the support plate 28. The drive shaft 24 includes a support plate connecting pin 24a for establishing a driving connection with the support plate 28. The support plate 28 includes a transverse top wall 28a which has a downwardly-extending boss like stub 28b. The stub includes an aperture 28c through which the drive shaft 24 extends and defines a spring seat 28d. A drive pin connecting groove 28e is provided on the drive side of the stub 28b for driving connection with the pin 24a. The support plate also includes a peripheral side wall 28f that terminates in an outwardly-extending flange 28g. The flange 28g may include one-half of a high-G port opening 28h.

The bowl cover 30, which is secured to the support plate 28, includes a transverse bottom wall portion 30a, and an upwardly-extending and outwardly-tapering side wall portion 30b which terminates in flange 30c that cooperates with the support plate flange 28g for securing the bowl 30 to the plate 28.

A conduit-receiving aperture 30d extends through the bottom wall, is aligned with the spin axis A--A and the low-G port 42 passes therethrough. The flange also includes a high-G port opening 30e which can be aligned with port opening 28h to form a high-G outlet. The cover 30 has a slot 30f which extends through the side wall from the flange to the port.

The mandrel 32 is positioned inside the cover 30, is shaped to generally conform to the interior of the rotor and has a bottom wall 32a, tapering side wall 32b and skirt 32c. The bottom wall is provided with a retainer recess 32d.

A spring-biasing mechanism is provided for urging the mandrel 32 toward the bowl 30 and against the chamber 40. The biasing mechanism includes a coiled compression spring 46 that surrounds the drive shaft 24, and is held in position at the top end by the stub 28b and spring seat 28d and at the bottom end by post-like keeper 48. The post 48 is an elongated, hollow, cylindrically-shaped member which seats in the mandrel recess 32d. The post includes a body portion 48a which fits within the spring 46 and an outwardly-extending flange or spring seat 48b on which the lower end of the spring rests. At the upper end, the post 48 has a top wall 48c with an aperture 48d through which the drive shaft 24 extends.

The drive shaft has at its lower end a retainer groove 24b which is positioned within the post 48 and a C-shaped retainer spring 24c which fits within the groove to retain the post 48 on the drive shaft and limits the extension of the spring 46.

Thus the biasing spring cooperates with the support plate stub 28b, post 48, drive shaft 24, pin 24a, and retainer 24c to urge the mandrel against the processing chamber 40 and toward the bowl 30. The maximum extension of the spring is controlled by the length of the drive shaft, between the pin 24a and retainer 24c, positioning of the retainer 24c, as shown in FIG. 2, mandrel engages the bowl 30 as shown in FIG. 3. The limit for compression of the spring 46 is defined by its solid height; abutment of the post 48 and the stub 28b; and/or engagement of the mandrel skirt 32d and support plate.

After assembly and installation of the chamber and closure of the housing, the biasing spring 46 urges the post 48 and, thus the mandrel, downwardly toward the bowl cover. The downward travel of the mandrel is limited by the restraint of the bowl and the

engagement of the shaft retainer 24c and post 48. In the fully extended position, the mandrel expresses substantially all fluid from the chamber, and, as shown, the chamber is prepared for receiving whole blood and component separation.

In operation the centrifuge is started with drives 22 and 23, and whole blood drawn from the donor is delivered to the chamber via the umbilicus 34. The whole blood entering the chamber causes the chamber to expand and push against the mandrel 32. As the chamber fills, it conforms to the shape of the mandrel and cover and urges the mandrel toward a retracted position. As the mandrel retracts, the post 48 is pushed upwardly, which causes the spring 46 to compress until the chamber is fully expanded or until the spring reaches its fully compressed solid height where the post abuts the support plate stub.

During separation, therapeutic components may be selectively withdrawn from the chamber through the low-G port 42 (or other ports if provided), thus decreasing the chamber volume. As the chamber volume decreases, the mandrel advances toward the cover, thus maintaining a conforming force against the chamber. As the mandrel advances and retracts in response to volume changes, the rim edge 40a of the chamber rolls up and down.

The chamber is sufficiently flexible so as to permit adjustment in volume without fracturing or tearing. It will be noted that the chamber walls may fold back against themselves during this process. At the end of the procedure, the chamber is removed by opening the housing and interior casing and then sliding the chamber off the mandrel. From the foregoing it will be seen that the apparatus disclosed herein

provides an apparatus for centrifugal apheresis in which the volume of the processing chamber is variable.

The shape of the bowl 30 and mandrel 32 cooperates with the chamber 40 to define a red blood cell collection volume and a plasma collection volume. Referring to FIG. 4, the plasma collection volume 50 is a cylindrical, disc-like space between the bowl bottom wall 30a and the mandrel bottom wall 32a. The blood cell collection volume is the annularly-shaped space 52 defined by the bowl side wall 30b and the mandrel side wall 32b. The blood cell collection volume 52 and plasma collection volume 50 are approximately equal as shown in the filled condition in FIG. 4. Furthermore, the volumes remain approximately equal to each other as the total volume of the chamber varies. In other words, throughout the range of chamber volumes from empty to full, the ratio of red blood cell or packed cell collection volume to plasma collection volume remains substantially constant at about 1:1.

Referring now to the packed cell collection volume 52, it is seen that during operation the red blood cells sediment toward or are driven toward the bowl wall 30b. This wall has a large surface area so as to maximize separation of the red blood cells.

The interface between the packed or red blood cell volume and plasma volume is a cylindrically-shaped surface, shown with dotted lines, which extends between the outer edge of the mandrel bottom wall 32a and the outer edge of the cover bottom wall 30a. During separation, a layer known as the "buffy layer" forms at that interface due to the separation of the platelets from the plasma. As shown, the interface surface area is

smaller than the RBC sedimentation surface. The reason the interface surface area is smaller is to minimize platelet separation during RBC collection.

In the embodiment shown herein, the RBC sedimentation surface area is greater than the platelet interface surface area. Desirably, the ratio of RBC surface area to interface surface area is at least 2:1 and even as great as 4:1. These relationships are selected so as to maximize RBC separation while minimizing platelet from plasma separation and loss into the buffy layer during RBC separation. During RBC separation fluids in the red blood cell volume 52 are exposed to high-G forces, while fluids in the plasma volume 50 are exposed to low-G forces.

In operation, the chamber is filled with whole blood and then subjected to a first or hard spin to obtain RBC separation. During this spin, red blood cells sediment and move radially outwardly and into the volume 52 where the cells then sediment toward the outer wall. During this operation plasma and platelets are displaced inwardly toward the plasma volume 50.

Platelet-rich plasma collects in the volume 50 and is subjected to much lower G or separation forces since its radial distance from the spin axis is less than that for the RBC's. Hence platelet separation from the plasma is minimized.

In one example, the chamber is filled with about 500 milliliters of whole blood having a hematocrit of 40 (i.e., 40 volume percent red blood cells). After spinning and separation, about 250 milliliters of packed red blood cells, with a hematocrit of 80, is obtained in the volume 52 and about 250 milliliters of platelet-rich plasma is available in the plasma volume 50.

Collection of the RBC or platelet-rich plasma can be effected through the high or low-G ports as desired. Thereafter, in subsequent separations platelets can be separated from the plasma so as to permit separate collection of platelets and platelet free plasma.

With respect to the pump, the patent to Cullis (US 4,734,089) discloses in FIG. 1, a centrifugal blood separator 10 that includes a bowl-shaped outer shell 11 dimensioned to fit within a similarly shaped recess in a rotatably driven casing (not shown in FIG. 1). A bowl-shaped inner shell 12 is disposed within the outer shell and forms therewith a centrifugal processing chamber 13 within which fractionation of whole blood takes place during rotation of the separator assembly. The rims of the two bowl-shaped shells are joined by cemented tongue-and-groove attachments to a flat cover member 14 which includes four red blood cell (RBC) collection ports 15 arranged in a first ring, and four white blood cell (WBC) collection ports 16 arranged at equal intervals in a second ring concentric with the first ring but of lesser diameter. The cover member also includes a plurality of apertures 17 at its center for establishing fluid communication with a rotating seal (not shown in FIG. 1) in a manner to be described presently. Each of the four collection ports 15 is connected to a length of tubing 18 which extends through an aperture 19 in cover member 14 and into the interior of the bowl-shaped inner shell 12. Similarly, each of the collection ports 16 is connected to a length of tubing 20 which extends through an aperture 21 and into the interior of the inner shell member.

Referring to FIG. 2, wherein the centrifugal separator unit is shown in conjunction with a rotating-seal type centrifugation apparatus, the outer shell 11 of the separator is

seated in a rotatably driven casing. The outer shell includes a thin upstanding cylindrical side wall portion 23 which terminates at its upward or downline end in an outwardly and then upwardly directed rim portion 24, and at its downward or upline end in an angular portion 25 joining a flat bottom wall portion 26. Similarly, the inside shell 12 includes a thin upstanding cylindrical side wall portion 27, an inwardly and then upwardly directed downline portion 28, and an angular portion 29 joining a flat bottom wall portion 30. The interior surfaces of the side wall portions 23 and 27 together define a separation channel 31 within processing chamber 13 within which RBC, WBC and plasma components are separated from the whole blood as it flows through the channel under the influence of a centrifugal force field. The rim portions 24 and 28 together define a region in chamber 13 of increased width wherein the blood components separated within channel 31 accumulate prior to withdrawal through collection ports 15 and 16.

An additional collection port 32 is provided in the rim portion 28 of inner shell 12 for the purpose of withdrawing plasma as it accumulates in chamber 13. This collection port is connected by a length of tubing 33 to a passageway 17a in top plate 14. Similarly, tubing 18 connects to a passageway 17b and tubing 20 connects to a passageway 17c in top plate 14. To provide means for admitting whole blood into separation channel 31 the inner shell 12 is provided with an inlet port 34 along the axis of rotation of casing 22. This port is connected by a tubing segment 35 to a passageway 17d in cover member 14. Additional apertures 36 may be provided through the bottom wall portions 26 and 30 of the inner and outer shells to facilitate installation of the

separator 10 in a seal-less type centrifugal apparatus in a manner to be described presently.

To provide fluid communication between the inlet and collection ports and the non-rotating portions of the flow system associated with the separator a rotating seal assembly 40 is provided on top plate 14 along the axis of rotation of casing 22. This seal assembly, which may be conventional in construction and operation, is mounted to top plate 14 by means of suitable fastening devices such as bolts 41. Referring to FIG. 2a, the rotating seal assembly consists of a rotating member 43 having a plurality of ring-shaped recessed 44 therein and a stationary member 45 having a plurality of communicating ring-shaped recessed 46 therein. Individual lands 47 are provided between respective ones of the recesses to maintain fluid isolation and additional irrigation and/or lubrication flow systems may be provided for improved operation in a manner well known in the art.

In practice, two passageways are provided in top plate 14 for each ring-shaped recess associated with a fractional component, and each of these passageways may in turn be connected by an appropriate Y-connector and appropriate lengths of connecting tubing to respective ones of the four collection ports associated with that fraction. These connections have not been shown in FIG. 2 for the sake of clarity.

The upper non-rotating portion 45 of the rotating seal assembly 40 is held in a stationary non-rotating position in compression-engagement with the lower rotating portion 43 by means of a retaining arm 48 mounted on the frame of the centrifugation apparatus. The lower rotating portion of the seal may consist of a polished ceramic disc

attached to member 14 by means of concentric O-rings which establish fluid communication between recessed 44 and appropriate ones of passageways 17. The upper stationary portion of the seal is formed of stainless steel lapped to insure perfect contact with the ceramic disc. Each of the ring-shaped recesses 46 thereon is connected by a passageway to a tubing port on the top of the disc.

Referring to FIG. 4, the RBC outlet port is connected by a tubing segment 50 to a peristaltic pump 51, the WBC outlet port is connected by a tubing segment 52 to a peristaltic pump 53, and the plasma outlet port is connected by a tubing segment 54 to a peristaltic pump 55. Whole blood is supplied to the inlet port by a tubing segment 56, to which said citrate dextrose (ACD) and Heparin are introduced through respective tubing segments 57 and 58 and a peristaltic pump 59. Saline is supplied to the rotating seal for isolation purposes through a tubing segment 60 and exhausted through a tubing segment 61. Saline is supplied to the seal for lubrication purposes by means of a tubing segment 62 and a peristaltic pump 63.

The white blood cells, red blood cells and plasma derived by the system may be pumped to respective collection bags for storage or may be returned to the donor as required. Various safety devices may be incorporated into the system to guard against leakage of air or undue temperature rise, or the occlusion of a vein in the donor.

Casing 22 is mounted on a drive shaft 64 which in turn is rotatably driven by means of a motor 65. In practice, this drive arrangement is designed and constructed to provide a very high degree of concentricity in the rotation of casing 22 to insure efficient operation of the separation process and efficient operation of the seal assembly 40.

In operation, casing 22 is rotated at approximately 800 rpm to establish a centrifugal force field across separation channel 31. The flow path is next primed with sterile saline solution for all air bubbles are removed by back-flushing the system through the WBC peristaltic pump 53. Whole blood is then admitted through tubing 56, rotating seal assembly 40, and tubing segment 35 to inlet port 34. The whole blood flows radially outwardly within chamber 13 and upwardly through separation channel 31. The centrifuge speed is now adjusted to achieve separation of the RBC, WBC and plasma components in the manner illustrated in FIG. 3. Separation begins as the blood flows up the side of the bowl toward the collection ports, the blood eventually separating into three concentric bands, with the dense red blood cells outermost, and the less-dense white blood cells, or buffy coat, at an intermediate radius and the least-dense plasma at the shortest radius. Platelets are generally distributed among all three regions, but can be concentrated somewhat by varying the centrifuge speed. Collection ports 15, 16 and 32 remove the components from processing chamber 13 for collection or return to the donor as desired.

Typically, the flow rate of the whole blood in chamber 13 is such that the residence time of the blood in the chamber is about three minutes. To insure that separation of the blood components will take place within this relatively short period of time it is necessary that the width of the separation channel 31 be very small, typically in the order of 1.5 mm or less. To obtain efficient separation of the blood components this dimension must be maintained with a high degree of concentricity so that the

components as they separate will flow upwardly to the collection area at the upper end of chamber 13.

To insure that the desired separation channel width is maintained with the desired degree of concentricity, the outer and/or inner shell members are provided, in accordance with the invention, with a plurality of inwardly-projecting integrally-molded spacing bosses 60 which bear against their opposing shell surface to maintain accurate spacing. To insure that these bosses will in fact be determinative of the inter-element spacing, the outer shell 11 is dimensioned such that when the separator unit 10 is seated in casing 22 the side walls of the outer shell are caused to deform inwardly to a slight extent. This deformation is sufficient to bring the spacing bosses 60 into engagement with their opposing wall surfaces and assure that the desired spacing is established and maintained. To facilitate insertion of the separator unit in casing 22 the outer shell is preferably formed with a slight inward taper, typically in the order of one degree, and the inner wall of casing 22 is formed with a complementarily taper.

The inner and outer shells are preferably molded of a polycarbonate plastic by means of conventional molding techniques. The sidewalls 23 and 27 of these shells may have a thickness of 0.125 inch to obtain the desired inward deformation when the separator is seated in casing 22. In a representative application, the separator 10 is formed with an outside diameter of approximately 6 inches and a height of approximately 4 inches. With a processing channel 31 1.5 mm wide, the processing chamber 13 has a volume of approximately 140 ml.

Once the various lengths of tubing have been installed during manufacture of the separator unit 10 the volume enclosed within the inner shell 12 may be filled with a foam material 66 to prevent accumulation of significant quantities of fluid within the chamber. This is a safety feature to insure that any leakage will be immediately evident to the operator and will not accumulate within the rotating bowl assembly.

Referring to FIG. 5, the centrifugal separator unit of the invention may also be utilized in conjunction with a seal-less centrifugation apparatus. Basically, this centrifugation apparatus includes a rotor drive assembly 70 to which a rotor assembly 71 is journaled by means of a hollow support shaft 72. The rotor drive assembly 70 is journaled to a stationary hub assembly 73 by means of a vertical drive shaft 74, and includes a guide sleeve 75.

The centrifugal processing chamber 10 of the invention is seated on the rotor assembly 71. Fluid communication is established between the separator unit, which rotates with the rotor assembly 71, and the non-rotating portion of the flow system, which may be identical to that shown in FIG. 4 except for the omission of the rotating seal member 40, by means of a four channel umbilical cable 76 which extends from a central location along the axis of rotation of the separator unit downwardly through the center of drive shaft 72, radially outwardly through guide sleeve 75 and upwardly to a fixed axially-aligned position established by a support arm 77. As described in the previously identified co-pending application Ser. No. 657,187, this routing of the umbilical cable 76, together with the rotor assembly 71 and rotor drive assembly 70 being driven in the same direction with a speed ratio of 2:1, establishes fluid

communication with centrifugal separator unit 10 without the cable becoming twisted. Instead, the umbilical cable is subjected only to flexing, or repeated partial twists about its axis through angles not in excess of 180 degrees, as the rotor assembly 71 rotates.

To obtain the desired 2:1 speed ratio between the rotor and rotor drive assembly two pairs of idler pulleys 78 are mounted on rotor drive assembly 70. A drive belt 79 is routed over these pulleys and around a stationary ring-type pulley 80 mounted on hub 73 at one end, and around a rotor drive pulley 81 carried on the bottom end of the rotor drive shaft 72 at its other end. As the rotor drive assembly 70 is rotated clockwise by means of a motor (not shown) driving drive shaft 74, drive belt 79 establishes a clockwise rotation of rotor assembly 71. Assuming that stationary pulley 80 and rotor drive pulley 81 have the same diameter, the rotational speed of rotor assembly 71 will be exactly twice that of rotor drive assembly 70, by reason of the combined effect of the direct 1:1 drive relationship established by pulleys 80 and 81 and the planetary motion of idler pulleys 78 about the rotational axis of rotor assembly 71.

In order that the centrifugal separator unit 10 can be seated in rotor assembly 71 the tubing segments 18, 20 and 33 associated with collection ports 15, 16 and 32 are routed through the center of the separator unit and down through apertures 36 in the bottom walls of the inner and outer shell members. A casing 82, which may be similar to casing 22 in all respects except for the provision of passageways 83 in its bottom wall for accommodating the connecting conduit segments, is mounted on rotor assembly 71 to receive the centrifugal separator unit. As with the previously described rotating seal embodiment, the wall of the outer shell is compressed by casing 82 to obtain a

separation channel 31 having a high degree of concentricity. The individual connecting tubing segments after passing through passageways 83 are joined into umbilical cable 76.

It is contemplated that the centrifugal separator unit 10 when intended for use in a seal-less centrifugation apparatus such as that shown in FIG. 5 would be manufactured as a single integral disposable unit in which umbilical cable 76 is included. To install this unit in the apparatus the free end of the umbilical cable could be threaded downwardly through the hollow rotor support shaft 72 and then radially outwardly and upwardly through sleeve 75 to support arm 77. The free end of the cable would then be pulled through until the separator unit was seated in casing 82. After use, the entire assembly would be removed from the apparatus and disposed of.

A centrifugal blood separator unit has been shown and described which provides efficient processing of blood into its constituent components. The separator unit can be economically formed by known molding techniques, and by reason of its low cost of manufacture, is ideally suited for disposable one-time use situations wherein the dangers of contamination to the donor from prior uses are completely avoided.

While particular embodiments of the invention have been shown and described, it will be obvious to those skilled in the art that changes and modifications may be made without departing from the invention in its broader aspects, and, therefore, the aim in the appended claims is to cover all such changes and modifications as fall within the true spirit and scope of the invention.

As is best shown in FIG. 3, a concentric lip 16L is provided having an inner surface aligned with the outer side of the white blood cell collection ports 16, and the adjacent bottom surface of the cover member 14 is provided with a concentric groove 16G into which the ports 16 open. The provision of this groove and lip has resulted in experimentally verified better separation of the red blood cells from the collected white blood cells.

It has been found in the bowl that only four spacer units 60 need to be employed and that the spacer flange between the inner and outer shells at 36 serves to not only fix the horizontal wall (bottom to top) spacing but also, to a significant degree, to fix the side wall spacing. In one embodiment only four spacers 60 were used successfully. These were positioned near the upper surface at equal spacing around the unit. One experimental bowl which was constructed in accordance with the present invention was made of polycarbonate molded in four parts and had an overall height of approximately four inches and a diameter of approximately six and one-eighth inches. This particular unit had a fluid capacity of only 143 ml which compares favorably with the prior art bowls of this type.

The shells 11 and 12 were of approximately 1/8 inch thickness and maintained a spacing of 0.050 inches. The outer shell, although reasonably rigid for handling purposes, was slightly out-of-round and under the increased forces of centrifugation might have deformed even more. However, with a true round casing 22, and of stainless steel, the outer shell was upon insertion caused to go into a true round and concentric shape.

Accordingly, it would have been obvious to one having ordinary skill in the art, at the time applicant's invention was made, to have provided the centrifuge of DE 2658926 A1 with a spring loaded plate as taught by Brown '691 for the purpose of controlling the volume of the separation chamber (Brown '691: col. 1, lines 65-68 and col. 4, lines 26-66) and to have provided the centrifuge of DE 2658926 A1 with a pump as taught by Cullis '089 for the purpose of positively transferring the materials to be separated to the centrifuge separation chamber and/or to positively remove the separated components form the separation chamber and transfer such components to storage receptacles or the donor (Cullis '089: col. 4, lines 28-48).

14. Claims 15 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 2658926 A1 in view of Brown (US 4,530,691) and Cullis (US 4,734,089) as applied to claims 1 and 16 above, and further in view of Muhlbock et al. (US 4,199,544).

DE 2658926 A1 in view of Brown (US 4,530,691) and Cullis (US 4,734,089) does not disclose the scale. The patent to Muhlbock et al. discloses a centrifuge apparatus for separating a sample and teaches a device for the reading-off of the measuring values without the use of troublesome intermediary or comparison means. A read-off scale is arranged along the vessel and in a fixed relation to the latter, and the junction between the columns serves as a marker coordinating with the read-off scale. By these means the measuring values to be determined can be read from or beside the capillary

tube or other vessel and the determination of the measurements thereby is greatly simplified and accelerated.

To prepare the measuring liquids for medical test purposes use is frequently made of a centrifuge, in the rotor of which a plurality of capillary tubes filled with test samples are clamped for centrifuging. The rotor holding the tubes is within a housing which can be closed by a pivoted cover. In this type of appliance it is advantageous, in accordance with a further feature of the invention, to make the optical enlarging means in the form of a lens which is arranged in the cover and can be brought with the latter into a predetermined read-off position, a read-off scale being provided in the rotor along each capillary tube. The predetermined read-off position is conveniently determined by a lateral arm of the cover which serves as an abutment cooperating with a counter abutment on the housing of the appliance. The lens can be secured in the cover as a separate element. The cover can however be made of transparent material and formed into a lens at a specific part of the material.

The centrifuge comprises a multi-part housing 10, installed in which is an electric driving motor for a rotor 12 of plate form. Four like capillary tubes 14 of predetermined content and predetermined lengths can be mounted radially in this rotor and clamped by means of a clamping button 16. Before the commencement of the centrifuging operation the rotor 12 with the capillary tubes 14 clamped therein is closed by a cover 18 pivotally mounted by pins 18a in two apertured lugs 10f of the housing 10. The cover 18 has a catch 18r which in the closed position of the cover engages resiliently with a catch projection 10r of the housing 10.

The cover is preferably made of transparent plastic material and a predetermined portion thereof is shaped to provide a magnifying lens 18p. The cover 18 is provided at one side wall with two downwardly extending projections 18b and 18c which are resilient in a direction radially with respect to the hinge pins 18a. Projection 18b cooperates with an abutment 10g of the stationary housing 10 and defines the read-off position of the cover 18 (FIGS. 1 and 2). The other projection 18c serves as a resilient end catch for retaining the cover 18 in its open position (FIGS. 3 and 4) when the capillary tubes are being inserted and clamped or being removed. Laterally alongside each capillary tube 14 in the rotor 12 is a scale 12s, for example impressed into the material of the rotor and made of a color which is readily visible. Measurement numbers in percentages are associated with the scale markings.

The transparent capillary tubes 14 used for a specific medical test are for example filled with the blood of the patients to be tested, clamped in the centrifuge, and subjected to a centrifuging operation. This produces in each capillary tube two columns of part components, namely an outwardly disposed column 14a with blood clots and an inner column 14b with blood plasma. The two columns are separated by a junction line 14t (FIG. 5) which is clearly visible. Since each capillary tube 14 is full, its total volume can be expressed as 100% for each complete length, further values being provided along the capillary tube 14 in the rotor 12 in like partial spacings within this area. Thus as soon as the cover 18 is brought into the read-off position according to FIGS. 1 and 2, the proportion of the two columns to the total volume of the capillary tube can be directly read-off. In the case of the capillary tube 14 which is in position "1" (FIG. 4) and which is

shown enlarged in FIG. 5, the measurement for the column 14a reads 51% and for column 14b correspondingly the value 49% of the total volume, thus making 100%.

The rotor 12 is turned by hand until all the capillary tubes are successively brought into the read-off position under the lens 18p, so that their values can be read-off and noted down.

Instead of the magnifying lens 18p being formed directly in the transparent plastic material of which the cover is made, a separate magnifying lens 180 of optical glass can be inserted in the cover 18 as illustrated in FIG. 6, if a particularly powerful optical enlargement is required.

It is also to be mentioned that the method of reading-off the percentage values in accordance with this invention can also be used for other medical test apparatus in which the values of the component part columns are to be measured in a vessel and automatically read-off.

Accordingly, it would have been obvious to one having ordinary skill in the art, at the time applicant's invention was made, to have provided the centrifuge of DE 2658926 A1 in view of Brown (US 4,530,691) and Cullis (US 4,734,089) with a scale as taught by Muhlbock et al. for the purpose of enabling an operator to determine the volume of material present in a separation chamber via the scale.

Allowable Subject Matter

15. Claim 36 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. Claims 40-41 are allowable over the prior art of record.

17. The following is an Examiner's statement of reasons for the indication of allowable subject matter:

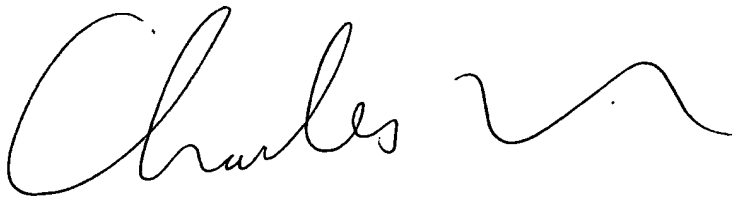
The prior art of record does not teach or fairly suggest the ball-screw actuator of claim 36 or the centrifuge with the recited cartridge of claim 40.

Conclusion

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles E. Cooley whose telephone number is (571) 272-1139. The examiner can normally be reached on Mon-Fri. All official facsimiles should be transmitted to the centralized fax receiving number 571-273-8300.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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Art Unit 1723

30 September 2005